

Application No. 09/818,943
Reply dated May 24, 2004
Response to Office Action dated February 23, 2004

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A method for producing a transgenic mouse, the method comprising the steps of:

a) introducing a transgenic DNA into a mouse cell, said transgenic DNA comprising a polynucleotide sequence operably linked to a suitable heart specific promoter that is capable of directing expression of the polynucleotide in heart, said polynucleotide encoding a polypeptide comprising SEQ ID NO:1 or SEQ ID NO:2;

b) allowing said cell from step a) to develop into a transgenic mouse,

wherein said cell of step a) is a pronuclei of a fertilized oocyte, said method further comprising implanting said fertilized oocyte into a pseudopregnant mouse; or

wherein said cell of step a) is an embryonic stem cell; said DNA is integrated into a genomic DNA of said embryonic stem cell; and said embryonic stem cell is introduced into a developing embryo, and

wherein the transgenic mouse overexpresses a polypeptide having platelet-derived growth factor C (PDGF-C) activity and develops myocyte hypertrophy or heart fibrosis during its life time.

2-4. (cancelled)

5. (currently amended) ~~The method of claim 1, wherein said promoter is A method for producing a transgenic mouse, the method comprising the steps of:~~

a) introducing a transgenic DNA into a mouse cell, said transgenic DNA comprising a polynucleotide sequence operably linked to an alpha-myosin heavy chain promoter, said polynucleotide encoding a polypeptide comprising SEQ ID NO:1 or SEQ ID NO:2;

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b) allowing said cell from step a) to develop into a transgenic mouse,
wherein said cell of step a) is a pronuclei of a fertilized oocyte, said method further
comprising implanting said fertilized oocyte into a pseudopregnant mouse; or
wherein said cell of step a) is an embryonic stem cell; said DNA is integrated into a
genomic DNA of said embryonic stem cell; and said embryonic stem cell is introduced
into a developing embryo, and
wherein the transgenic mouse overexpresses a polypeptide having platelet-derived
growth factor C (PDGF-C) activity and develops myocyte hypertrophy or heart fibrosis
during its life time an alpha-myosin heavy chain promoter.

6. (previously presented) The method of Claim 1, wherein said transgenic DNA is operably linked to an epitope tag.

7. (original) The method of Claim 6, wherein the epitope tag is c-myc.

8. (original) The method of Claim 1, wherein said transgenic DNA is operably linked to a marker sequence.

9. (previously presented) The mouse produced by the method of claim 1.

10-11. (cancelled)

12. (currently amended) A transgenic mouse that is a descendant from the mouse according to claim 9, wherein the transgenic mouse overexpresses a polypeptide having platelet-derived growth factor C (PDGF-C) activity and develops myocyte hypertrophy or heart fibrosis during its life time.

13. (cancelled)

14. (previously presented) The mouse according to Claim 9, wherein the mouse is homozygous with regard to the transgenic DNA.

15. (currently amended) A cell isolated from a the mouse according to claim 9.

16-17. (cancelled)

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18. (currently amended) A fertilized mouse oocyte containing a polynucleotide molecule that comprises a heart specific promoter that is capable of directing expression of the polynucleotide in heart and that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

19. (currently amended) A transgenic mouse embryonic stem cell containing a polynucleotide molecule that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

20. (currently amended) A method for identifying a compound as a PDGF-C antagonist, said method comprising:

introducing a candidate compound into a the transgenic mouse according to Claim 9; and

monitoring a biological activity of PDGF-C in said mouse;

wherein inhibition of the PDGF-C biological activity indicates that the candidate compound is a PDGF-C antagonist.

21. (cancelled)

22. (currently amended) A method for identifying a compound as a PDGF-C antagonist, said method comprising the steps of:

exposing to said compound a test cell isolated from a the transgenic mouse according to Claim 9;

assaying an effect of said compound on a PDGF-C activity of said test cell *in vitro*;

comparing PDGF-C activity in a control cell not exposed to said compound, and

identifying said compound as a PDGF-C antagonist where the PDGF-C biological activity of said test cell is altered as compared to the PDGF-C activity of the control cell.

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23. (currently amended) A method of screening for a compound for inhibition of hypertrophy, comprising the steps of:

administering a candidate compound to a test transgenic mouse according to Claim 9; and

monitoring cardiac development of said test mouse;

monitoring cardiac development of a control transgenic mouse according to Claim 9 not exposed to said candidate compound; and

wherein inhibition of cardiac development in said test mouse when compared to the a control transgenic mouse in the absence of said candidate compound indicates that the candidate compound inhibits hypertrophy.

24. (currently amended) A method of screening for a compound for inhibition of fibrosis, comprising the steps of:

administering a candidate compound to a test transgenic mouse according to Claim 9; and

monitoring cardiac development of said test mouse;

monitoring cardiac development of a control mouse according to Claim 9 not exposed to said candidate compound; and

wherein inhibition of cardiac development in the test moust when compared to the a control transgenic mouse in the absence of said candidate compound indicates that the candidate compound inhibits fibrosis.

25. (currently amended) A The transgenic mouse according to Claim 9, wherein the mouse is heterozygous with regard to the transgenic DNA encoding a polypeptide comprising the amino acid sequence SEQ ID NO:1 or SEQ ID NO:2.

26-28. (cancelled)

29. (currently amended) A method for producing a transgenic mouse, the method comprising the steps of:

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a) introducing a transgenic DNA into a mouse embryonic stem cell, said transgenic DNA comprising a polynucleotide sequence operably linked to a suitable promoter, said polynucleotide encoding a polypeptide comprising the sequence of SEQ ID NO:1 or SEQ ID NO:2, and

b) introducing said embryonic stem cell into a developing embryo which is allowed to develop into a transgenic mouse,

wherein the transgenic mouse overexpresses a polypeptide having platelet-derived growth factor C (PDGF-C) activity and develops hypertrophy or fibrosis in its heart at least one of its organs in its life time.